Community-Based Therapeutic Drug Monitoring
Useful Development or Unnecessary Distraction?

Mark Campbell
Regional Drug and Therapeutics Centre, Wolfson Unit, Newcastle upon Tyne, England

The application of clinical pharmacokinetics to the routine monitoring of drug therapy has, with few exceptions, developed mainly in hospital practice. Despite over 20 years of experience, debate continues over the place of routine therapeutic drug monitoring (TDM).[1] Although biochemical, haematological and pathological testing is carried out commonly by primary care clinicians, they have not, despite similarly accessible hospital testing facilities, been involved routinely with TDM. Recently, however, the development of nonlaboratory assay devices has led to the possibility of community-based drug-concentration monitoring activities. In the UK, such activities have been promoted as one possible facet of the extended role of community pharmacists.[2]

1. Development of Assay Technology

Several different systems are available that require minimal instrumentation and that can be used by nonlaboratory personnel. For example, the 'Acculevel' is a hand-held assay, with yield accuracy and specificity comparable to those of established laboratory methods for phenytoin, phenobarbital (phenobarbitone) and theophylline.[3] However, the manufacturers have withdrawn the 'Acculevel' system from the UK market because of low demand.

2. Therapeutic Monitoring in the Community

For drugs such as phenytoin, digoxin, theophylline and lithium, there are few published data upon which to assess the frequency of monitoring in community-based patients. The need for monitoring, however, is evident. Medication problems related to poor monitoring have, for example, been reported in patients with epilepsy.[4,5] Table I summarises published studies in which serum concentrations were measured in 'typical' community-based patients taking theophylline. Overall, the majority of patients had concentrations that would be considered to be subtherapeutic. Two of these studies were also designed to optimise the treatment of individual patients.[14,16] Maguire and McElnay[14] reported that, after dose adjustment, the proportion of patients with concentrations in the range from 10 to 20 mg/L had increased from 14 to 68%, while the corresponding proportion reported by Neville and McDevitt[16] increased from 20 to 67%. These investigators described this task as 'laborious but not difficult'.[16]

3. Developing Community-Based Therapeutic Drug Monitoring

Community-based TDM should result in a higher proportion of patients receiving effective drug therapy. In particular there should be:
fewer episodes of toxicity;
an increase in compliance; and
a general increase in practitioner’s interest in the
medication review.

These advantages are offset by the investment
in resources necessary to undertake more frequent
monitoring. Such monitoring would also require
agreement on guidelines, for example for patients
who have improved clinically on therapy, but have
low drug concentrations. The devolution of respon­sibility to other healthcare workers, such as phar­
macists, also has important training and medico­
legal implications. Moreover, there are some drugs
(such as cyclosporin) for which monitoring should
be undertaken by specialists rather than general
practitioners.

The interest in community-based monitoring is
dependent upon 4 key components:
available technologies;
evidence of problems in drug therapy that might
be addressed by therapeutic monitoring;
pharmacokinetic expertise; and
widespread interest by enthusiastic community­
based healthcare professionals (and patients).

Reliable computer-based models for dosage de­
termination and noninstrumented assay techniques
go some way to providing 2 of these components.
However, there are almost no data by which to
judge whether the final component would (or even
should) be desirable or achievable, at least among
conventional family physicians. There is, in ad­
dition, a serious risk that the promotion of commu­
nity-based TDM, based upon a conventional strat­
egy of target serum concentrations, would detract
from the global aim of improving prescribing and
drug therapy.

For example, about 200 000 patients (based on
prescription data) are treated each year in England
with theophylline. Although studies admittedly in­
volve small numbers of patients, results suggest
that about three-quarters of these have suboptimal
serum concentrations. At a time when the place of
theophylline in the treatment of respiratory disease
and its therapeutic range are a matter of debate, it
makes little sense to attempt dosage adjustment to

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Age (years)</th>
<th>No. of drug concentrations</th>
<th>Theophylline serum concentration (mg/L)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>0-10</td>
<td>10-20</td>
</tr>
<tr>
<td>NS</td>
<td>NS</td>
<td>179</td>
<td>94</td>
<td>73</td>
</tr>
<tr>
<td>20</td>
<td>NS</td>
<td>20</td>
<td>18</td>
<td>2</td>
</tr>
<tr>
<td>150</td>
<td>6-90</td>
<td>150</td>
<td>113</td>
<td>36</td>
</tr>
<tr>
<td>33</td>
<td>43-86</td>
<td>33</td>
<td>21</td>
<td>12</td>
</tr>
<tr>
<td>13</td>
<td>NS</td>
<td>18</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>16</td>
<td>18-84</td>
<td>16</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>37</td>
<td>16-90</td>
<td>37</td>
<td>28</td>
<td>9</td>
</tr>
<tr>
<td>46</td>
<td>55 (mean age)</td>
<td>46</td>
<td>34</td>
<td>8</td>
</tr>
<tr>
<td>22</td>
<td>NS</td>
<td>22</td>
<td>18</td>
<td>3</td>
</tr>
<tr>
<td>53</td>
<td>5-83</td>
<td>103</td>
<td>60</td>
<td>36</td>
</tr>
<tr>
<td>55</td>
<td>NS</td>
<td>55</td>
<td>44</td>
<td>11</td>
</tr>
<tr>
<td>45</td>
<td>24-86</td>
<td>45</td>
<td>34</td>
<td>10</td>
</tr>
</tbody>
</table>

Totals (% of total) 724 (100%) 477 (66%) 218 (30%) 29 (4%)

a In the 1-year study period, there were 42 patients taking theophylline who did not have a serum concentration measured.
b Therapeutic concentrations were achieved in 15 (68%) of patients.
c Before dosage adjustment.
d Therapeutic concentrations were achieved in 37 patients.
e Serum theophylline concentrations were remeasured twice and found to vary significantly; however, the proportion of concentrations in each band was similar.

Abbreviation: NS = not stated.

© Adis International Limited. All rights reserved.